PHARMACEUTICAL SCIENCES

ACCEPTANCE FOR FILING AND REVIEW OF AADA'S ABSENT APPROVAL OF THE REFERENCED BULK ANTIBIOTIC

CONTENTS

PURPOSE

- To clarify the Office of Generic Drug (OGD)'s policy toward acceptance for filing and review of Abbreviated Antibiotic Applications (AADA's) for finished dosage forms where the bulk antibiotic referenced in such applications is not approved.

BACKGROUND

- The antibiotic regulations require that dosage form products may use only a bulk active ingredient that is the subject of an approved antibiotic drug application. This is in contrast with non-antibiotic drug products where the active ingredient is not the subject of a special application process. For non-antibiotic drugs, the active ingredient may be the subject of a Drug Master File or may be described as an integral part of the drug product application.

- It has been the practice of the Antibiotic Review Branch to accept for filing AADA's for dosage form products if the bulk-antibiotic application referenced had been submitted for review. As a consequence it is quite possible that the review of dosage form applications may arrive at a point of being approvable before the referenced bulk application is approved.

- It must be recognized that the dosage-form AADA applicants are taking a considerable risk if they base their applications upon an unapproved source of bulk antibiotic. Should the bulk not be approved, the dosage-form applicants may have to begin the application development process over and generate new supporting data, or should considerable changes be required in the bulk-drug application before approval, data such as bioequivalence and stability may have to be regenerated for incorporation into the antibiotic drug product application.

POLICY AND PROCEDURE

- Consistent with our commitment to facilitate the timely availability of generic antibiotic products, provided that the referenced bulk-antibiotic application has been submitted to the agency for review, the OGD's policy will remain to receive and accept for filing otherwise complete, reviewable abbreviated antibiotic dosage-form applications that reference as yet unapproved, bulk-antibiotic applications.

- Such AADA's will be located in the work queue at the appropriate point determined by their date of receipt and acceptance. They will be reviewed in accordance with the OGD's "first-in, first-reviewed" policy (see MAPP 5240.3).

- If an applicant wishes to use an unapproved bulk drug source for a bioequivalent study, an Investigational New Drug Application (IND) is required since the unapproved bulk drug may not be placed into interstate commerce for investigational purposes without either an approval or an exemption.

- In the event such a dosage form application arrives at a point of completion where a not approvable (NA) letter is developed based upon deficiencies specific to the content of the application - and the referenced bulk-antibiotic application has not yet been approved - the NA letter may issue but should include an additional statement as follows:

  > In addition to the above cited deficiencies, please note that the referenced bulk-antibiotic application has not yet been approved. Until it is approved, this application will remain not approvable. You should contact the referenced bulk-antibiotic applicant; and once the bulk applicant confirms that the application under consideration has been approved, you may amend your application to advise FDA accordingly. You may independently seek to address all the deficiencies within your control.

- In the event such a dosage-form AADA arrives at a point of completion where all deficiencies have been satisfactorily addressed except that the referenced bulk-antibiotic application has not yet been approved, an NA letter which includes the following statement should be prepared:

  > The referenced application for the bulk-antibiotic has not yet been approved. Until it is, this application will remain not approvable. Once the referenced bulk-antibiotic applicant confirms that their application has been approved, you may amend your application to advise FDA accordingly.

- It is not the responsibility of the OGD to advise antibiotic dosage-form applicants that have received an NA letter citing the deficiency under POLICY AND PROCEDURE, paragraphs 4 and 5 above that the referenced bulk-antibiotic

application has been approved.

EFFECTIVE DATE

- This guide is effective upon date of publication.